Reactions of 2-Methylene-1,3-cyclopentanedione with Electron-Rich Alkenes

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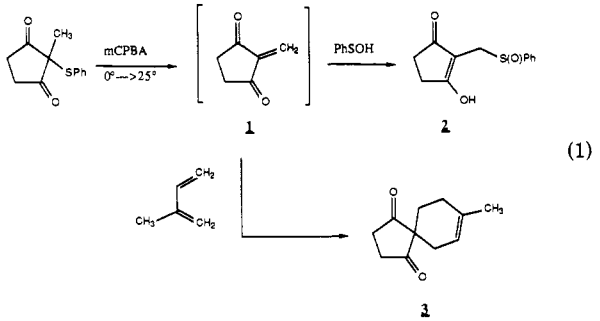
Treatment of 2-[(phenylsulfinyl)methyl]-1,3-cyclopentanedione with pyridine leads to the generation of the title compound (1). Under these conditions, 1 reacts rapidly and efficiently with enamines and trimethylsilyl enol ethers to give products of Michael addition to the enedione system. Alkyl vinyl ethers add to 1 in a cycloaddition process leading to fused dihydropyrans. Labeling studies establish that the cycloaddition is >95% stereospecific. The possible involvement of a zwitterionic pathway in the cycloaddition was ruled out on the basis of a negligible effect of solvent polarity on reaction rate. The Michael addition reactions show some mechanistic diversity, with both zwitterionic and cycloaddition processes indicated, depending on the alkene.

The title compound (1) is parent of a class of exceedingly reactive molecules, namely, the 2-alkylidene-1,3-cyclopentanediones. The unusual, doubly *s*-cis enedione chromophore present in alkylidene derivatives of cyclic β-diketones, as well as the great synthetic potential of such well-functionalized ring systems, has attracted interest in their chemistry.[1] These compounds are more reactive than their acyclic counterparts and cannot be prepared in general by classical Knoevenagel condensation. Recently, we demonstrated that 2-alkylidene-1,3-cyclopentanediones could be prepared under mild conditions by sulfoxide elimination from the corresponding 2-alkyl-2-(phenylthio)-1,3-cyclopentanedione (eq 1).[2] In the case of 1, the



(1)

enedione does not accumulate. Instead, conjugate addition of the nascent benzenesulfenic acid occurs under the conditions of the elimination so that 2 is the isolated product. Nevertheless, the transient 1 can be engaged in useful chemistry, for example, the Diels–Alder cycloaddition with isoprene.

Cyclic β-diketones are particularly effective at stabilizing anions (the pK_a of 1,3-cyclopentanedione is 4.6).[3] Thus, the carbon–carbon double bond of 1 is highly polarized, and we can expect facile addition of even weak nucleophiles to the enedione system (cf. 1 → 2). Indeed, we have shown that 1 is a potent electrophile toward anthracene, even without added catalyst.[4] Conjugate additions to 1 lead to more elaborate 2-alkyl-1,3-cyclopentanediones, compounds of established synthetic utility.[5] These might be prepared by C-alkylation of 1,3-cyclopentanedione, a process that is plagued by competing (often dominant) O-alkylation.[6] We have been interested in developing nucleophile additions to 1 as a conceptually new route to functionalized 2-alkyl-1,3-cyclopentanedione and report here the results of our study.

We chose to focus on the additions of carbon nucleophiles, specifically enamines and enol ethers. Unfortunately, these acid-labile species were not stable under the conditions used to prepare 1. Thus, attempts to use near-stoichiometric amounts of silyl enol ether to trap 1 in situ invariably led to desilylation without substantial combination with 1. The use of large excesses of the enol ether was somewhat more successful in producing addition product, but this is wasteful of enol ether and increase the problems of isolation and purification. Efficient reaction would require a new method for generating 1, under nonacidic conditions. Such a method evolved during the characterization of 2. Like most enolized cyclopentanediones, 2 is quite insoluble in nonpolar organic solvents. In order to obtain NMR spectra of these compounds, we adopt the simple expedient of adding some pyridine-d_5 to the $CDCl_3$ solvent. Deprotonation by the base disrupts the polymeric, H-bonded array of the enolized 1,3-cyclopentanediones, bringing them into solution. In the case of 2, however, dissolution was accompanied by development of a bright yellow color, which signalled some kind of reaction. The ^1H NMR spectrum of this solution ($CDCl_3$, py-d_5) exhibited, in addition to phenyl signals, a 2-H singlet at δ 5.30 and a 4-H singlet at δ 2.40. Addition of isoprene causes the color to fade within 1 h, at which time the spiro dione 3 can be isolated in >60% yield. We take these results to indicate the presence of 1 in pyridine solutions of 2. The NMR shifts are not consistent with 1 as the dominant species[7] but likely reflect a weighted average of a mobile equilibrium between 1 and 2. Indeed, the chemical shift for the exocyclic CH_2 in the pyridine solution is intermediate between that expected for 1 and that observed for static 2 in acetone-d_6, and the signal lacks the diastereotopic differentiation seen in the latter solvent.

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(2) (a) Eaton, P. E.; Bunnelle, W. H. *Tetrahedron Lett.* **1984**, *25*, 23. (b) Eaton, P. E.; Bunnelle, W. H.; Engel, P. *Can. J. Chem.* **1984**, *62*, 2612.

(3) Boothe, J. H.; Wilkinson, R. G.; Kushner, S.; Williams, J. H. *J. Am. Chem. Soc.* **1953**, *75*, 1732.

(4) Bunnelle, W. H.; Shangraw, W. R. *Tetrahedron* **1987**, *43*, 2005.

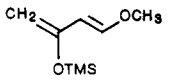
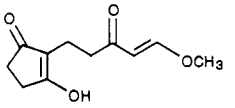
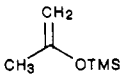
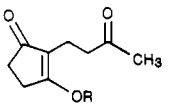
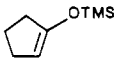
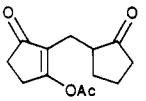
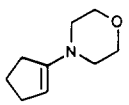
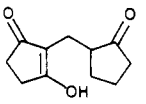
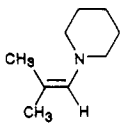
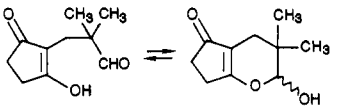
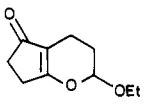
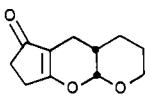
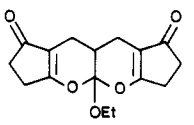
(5) (a) Hirai, K.; Suzuki, H.; Kashigawi, H.; Moro-Oka, Y.; Ikawa, T. *Chem. Lett.* **1982**, 23. (b) Yura, Y.; Ide, J. *Chem. Pharm. Bull.* **1969**, *17*, 408. (c) Schick, H.; Lehmann, G.; Hilgetag, G. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 80. (d) Akhrem, A. A.; Titov, Y. A. *Total Steroid Synthesis*; Plenum: New York, 1970; pp 149–175. (e) Ellison, R. A. *Synthesis* **1973**, 397.

(6) McIntosh, J. M.; Beaumier, P. M. *Can. J. Chem.* **1973**, *51*, 843 and references therein.

(7) β-Hydrogens in alkylidene dicarbonyl systems have NMR resonances in the 7.1–7.5 ppm range. See ref 1a,b,e.

0022-3263/88/1953-4038$01.50/0

Table I

alkene	time (h)	product	yield, %
	0.5	 **5**	73
	2	 **6**, R=H **8**, R=Ac	49
	2	 **9**	55
	0.15	 **7**	68
	0.15	 **10** **11**	60
CH_2=$CHOCH_2CH_3$	2.5	 **14**	70
	24	 **15**	60
HC≡$COCH_2CH_3$	3	 **18**	71

Of course, it is possible that some other species, for example, the pyridine adduct to **1**, is also involved. It is worth noting here that we have so far been unable to recover **2** from its solution in pyridine–$CHCl_3$. In any case, it is clear that this solution of **2** is a useful source of 2-methylene-1,3-cyclopentanedione that permits the study of acid-sensitive coreactants.

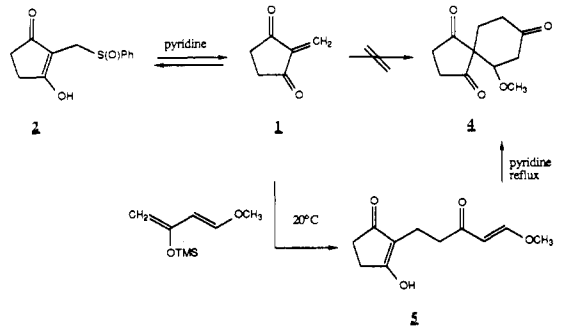
We looked first at the reaction of **2** with Danishefsky's diene[8] under these conditions. We anticipated that Diels–Alder cycloaddition would provide access to the functionalized spiro[4.5]decane **4**, but this product was not formed at room temperature. Instead, NMR monitoring of the reaction mixture indicated a rapid, clean conversion of the starting materials to **5**, the product of Michael addition of the silyl enol ether to enedione **1**. No other intermediates were detected. The facility of this reaction is remarkable. Conjugate additions of silyl enol ethers generally require Lewis acid catalysis, elevated temperatures, or high pressures.[9] In this case, the exceptional electrophilicity of **1** results in complete reaction within 15 min at 20 °C, without added catalyst. The product **5**, isolated in 73% yield, corresponds to that of the first stage in a decidedly nonconcerted cycloaddition. In fact, it proved possible to complete this process. Treatment of **5** in refluxing pyridine effects intramolecular Michael closure to give **4** (eq 2).

Simpler trimethylsilyl enol ethers also react easily with **1**. Thus, the TMS enol ethers of acetone and cyclopentanone lead to **6** and **7**, respectively, in satisfactory yields (see Table I). In these instances, product purification was facilitated by conversion to the corresponding enol acetates **8** and **9**. The starting enol ether is consumed efficiently—we typically use 1.2 molar equiv (vs **2**), and the reaction is complete within 2 h at 20 °C.

Enamines are more nucleophilic than TMS enol ethers. Consistent with this, we find that the reaction of enamines

(8) Danishefsky, S.; Kitahra, T.; Schuda, P. F. *Org. Synth.* **1983**, *61*, 147.

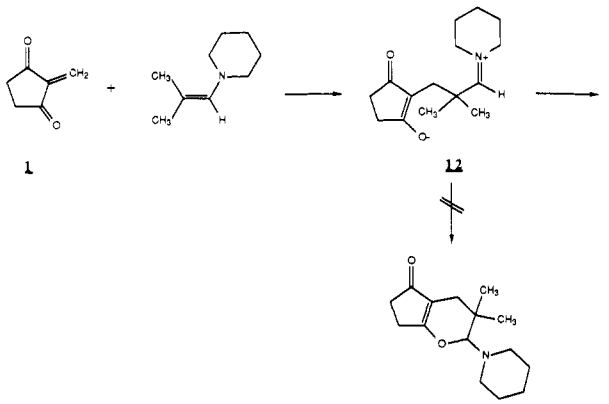
(9) (a) Narasaka, K.; Soai, K.; Aikawa, Y.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 779. (b) Kita, Y.; Sagawa, J.; Haruta, J.; Fujii, T.; Tamura, Y. *Tetrahedron Lett.* **1980**, *21*, 3779. (c) Bunce, R. A.; Schlect, M. F.; Dauben, W. G.; Heathcock, C. H. *Tetrahedron Lett.* **1983**, *24*, 4943. (d) Yamamoto, Y.; Maruyama, K.; Matsumoto, K. *Tetrahedron Lett.* **1984**, *25*, 1075.



2 1 4 5 (2)

with 1 is more rapid (<10 min at 20 °C) than that for the corresponding TMS enol ethers. Once again, the products, isolated after aqueous workup, are those of Michael addition. Particularly noteworthy is the facile reaction of *N*-isobutenylpiperidine with 1, where the formation of a quaternary carbon center is easily achieved. NMR analysis of this product shows that it exists largely in the cyclic, hemiacetal form 11 (anomeric H at δ 5.28), but rapid equilibration to the open, symmetrical aldehyde **10** is indicated by the NMR equivalence of the geminal methyl groups.

When these Michael additions are followed by NMR, some variations in the mechanistic details emerge. Thus, the initially observed product between enamines and 1 appears to be the iminium zwitterion, for example, **12** (eq 3). Specifically, the NMR spectrum of the crude reaction

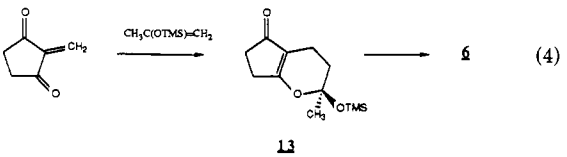


(3)

mixture shows a sharp singlet for equivalent methyl groups in **12** and the iminium CH at δ 9.45.[10] Interestingly, we find no clear evidence for closure to the corresponding hemiaminal as has sometimes been observed.[11] Here, the especially low basicity of the cyclic β-diketonate may work against such a process. On the other hand, we cannot exclude the possibility that the hemiaminal is in fact the initial product (via cycloaddition) but rapidly opens to the zwitterion **12**.

For the reaction 1 with the Danishefsky diene, the only observable product is **5**. Quite probably, a zwitterionic intermediate analogous to **12** is so readily desilylated that it does not accumulate to detectable levels. Interestingly, 2-[(trimethylsilyl)oxy]propene reacts with 1 to give initially the cyclic acetal **13**, detectable by NMR. This is not isolable, however, and suffers ready desilylation/ring opening to **6** on workup (eq 4).

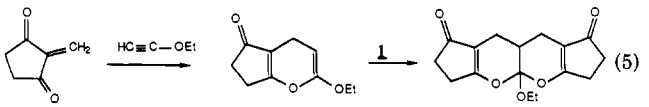
In contrast to these conjugate addition processes, the reaction of 1 with alkyl enol ethers leads to cycloadducts,



13 6 (4)

corresponding to hetero-Diels–Alder addition across the *s*-cis enone of 1. Thus, addition of ethyl vinyl ether to a $CHCl_3$/pyridine solution of **2** leads, within 3 h, to a 70% yield of cycloadduct **14**. The corresponding reaction with dihydropyran is somewhat slower, but a good yield of cycloadduct is obtained after 24 h at 20 °C. In this case, only a single diastereomer of the product (**15**) was detected. The vicinal coupling constant to the anomeric proton (δ 5.43, d, J = 2.6 Hz) is too small for a trans-diaxial interaction and is consistently only with a cis ring fusion.

Twofold cycloaddition of 1 occurs with ethoxyacetylene, so that the isolated product is the tetracyclic ortho ester **18**. We have been unable to adjust reaction conditions so that the presumed intermediate 1:1 adduct (**17**) could be observed. Apparently, the ketene acetal moiety within **17** competes effectively, even with excess ethoxyacetylene, for the available enedione 1 (eq 5).



1 17 18 (5)

These cycloadditions are well precedented for similar unsaturated carbonyl compounds. They have typically been formulated as Diels–Alder additions with inverse electron demand and frequently appear to be concerted processes.[1e,11-14] In some cases, however, evidence points to a two-step process involving a zwitterionic intermediate.[14] Because of the apparent involvement of zwitterions in the reaction of 1 with some silyl enol ethers and enamines, further study of the mechanism of cycloaddition of 1 with vinyl ethers was warranted.

We have no evidence to suggest a two-step mechanism for the cycloaddition of vinyl ethers with 1. NMR monitoring of the reaction indicates clean conversion of the starting materials to products, with no detectable intermediates. No 2 + 2 adducts, which might be expected for a zwitterionic process, are obtained.

A concerted cycloaddition requires stereospecificity. Therefore, the retention of alkene stereochemistry in the formation of **15** was intriguing. On the other hand, the cis geometry is preferred for **15** due to the stabilizing anomeric effect when the oxygen substituent is axial. Moreover, the limited flexibility of a zwitterion derived from dihydropyran and 1 might well favor kinetic closure to the cis-fused product, and so the exclusive formation of **15** could not be taken as strong evidence for a concerted process. A less biased stereochemical probe was required. The stereolabeled ethyl vinyl ethers **16b,c** have been reported[15] and were used in this study. Cycloaddition of

(10) Merenyi, R. In *Iminium Salts in Organic Chemistry*; Bohme, H., Viehe, H. G., Eds.; Adv. Org. Chem. Series; Vol. 9, Part 1; Taylor, E. C., Ed.; Wiley: New York, 1976; pp 23–105.

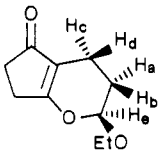
(11) (a) Snider, B. B. *Tetrahedron Lett.* **1980**, *21*, 1133. (b) Snider, B. B.; Roush, D. M.; Killinger, T. A. *J. Am. Chem. Soc.* **1979**, *101*, 6023.

(12) (a) Desimoni, G.; Tacconi, G. *Chem. Rev.* **1975**, *75*, 651. (b) Schmidt, R. R. *Acc. Chem. Res.* **1986**, *19*, 250. (c) Dvorak, D.; Arnold, Z. *Tetrahedron Lett.* **1982**, *23*, 4401. (d) Yamauchi, M.; Katayama, S.; Baba, O.; Watanabe, T. *J. Chem. Soc., Chem. Commun.* **1983**, 281. (e) Wallace, T. W. *J. Chem. Soc., Chem. Commun.* **1983**, 228. (f) John, R. A.; Schmid, V.; Wyler, H. *Helv. Chim. Acta* **1987**, *70*, 600.

(13) Tietze, L. F. In *Selectivity—A Goal for Synthetic Efficiency*; Bartmann, W., Trost, B. M., Eds.; Verlag Chemie: Weinheim, 1984; pp 299–316, and referneces therein.

(14) (a) Padias, A. B.; Hedrick, S. T.; Hall, H. K., Jr. *J. Org. Chem.* **1983**, *48*, 3787. (b) Hall, H. K., Jr. Padias, A. B.; Way, T.-F.; Bergami, B. *J. Org. Chem.* **1987**, *52*, 5528.

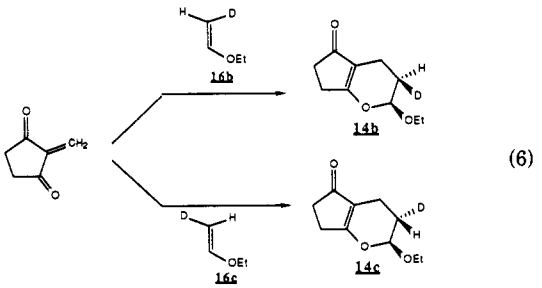
Table II



14a

labeled atom	chem shift (∂, $CDCl_3$), ppm	labeled atom	chem shift (∂, $CDCl_3$), ppm
Ha	1.75	Hd	2.24
Hb	1.96	He	5.33
Hc	2.22		
couplng interactn	J value (Hz)	couplng interactn	J value (Hz)
Ha–Hb	−13.2	Ha–Hc	5.2
Ha–Hd	10.3	Ha–He	2.6
Hb–Hc	6.6	Hb–Hd	3.4
Hb–He	3.7	Hc–Hd	−18.7
Hc–He	0	Hd–He	0

these with 1 would lead to **14b,c**, differing in the stereochemistry of the label relative to the ethoxy group, and so a method had to be found to distinguish between these two possibilities (eq 6). For **14a**, the proton signals in



(6)

question are completely resolved in the NMR at 300 MHz. The small couplings to the anomeric proton (∂ 5.33, dd, J = 3.7, 2.6 Hz) indicate that the ethoxy group occupies a pseudoaxial orientation, in accord with the anomeric stabilization. The adjacent methylene group gives rise to signals centered at ∂ 1.96 and 1.75. The multiplet pattern of these protons could be simulated satisfactorily by using the coupling constants listed in Table II. The upfield signal with a large (10.3 Hz) vicinal coupling was assigned to the pseudoaxial proton H_a, that is, trans to the ethoxy group. The downfield signal was characterized by smaller vicinal couplings, consistent with the equatorial placement of H_b. With these assignments, the stereochemical outcome of the reaction between 1 and the labeled ethers **16b** and **16c** could be assessed.

In the event, the reaction was entirely stereospecific. Thus, the product with **16b** gave an NMR spectrum where the signal at ∂ 1.96 had diminished; that at ∂ 1.75 showed the lessened coupling of the geminal D atom. Complementary results were obtained on cycloaddition of 1 with **16c**: the signal for H_a was attenuated, and there was contraction of the splitting envelope for H_b, indicating that the deuterium label occupied the pseudoaxial (trans to OEt) site. Unfortunately, in both experiments some residual proton signal (ca. 10%) was observed for the respective deuterium-substituted sites. This could be traced to the presence of all-protio ethyl vinyl ether in the samples of **16b,c** which were used. That these residual signals were not due to loss of stereochemical integrity in the cycloaddition was supported by analysis of the spin–spin coupling patterns. In each case, the splittings were consistent with a geminal proton–proton coupling (as for **14a**, see Table II) and not with coupling to a geminal deuterium neighbor. Nevertheless, the presence of the residual signal complicated our efforts to establish a lower limit to the stereospecificity of the cycloaddition. Fortunately, we were able to accomplish this by taking recourse to ^2H NMR. The ^2H signals for **14b** (downfield) and **14c** (upfield) are resolved and provide a measure of the reaction stereospecificity. Thus, the reaction product (**14c**) from 1 and **16c** gives a ^2H NMR spectrum consisting of a single line, upfield from that of **14b**. Integration establishes that this sample contains less than 5% of **14b**, and therefore the reaction is >95% stereospecific.

While stereospecificity is a necessary result of a concerted cycloaddition, it is not by itself a sufficient test of the mechanism. It is well known that two-step, zwitterionic processes are subject to rate acceleration in polar solvents. We have carried out the reaction between 1 and ethyl vinyl ether in $CDCl_3$ and CD_3CN (each with ca. 5% pyridine-d_5). By NMR monitoring of the reactions, it was established that no dramatic rate increase (less than 2-fold) accompanied the reaction in acetonitrile when compared to chloroform. On this basis, we consider the involvement of zwitterions to be quite unlikely and therefore favor a concerted mechanism for this cycloaddition process.

In summary, we report a new method for the generation of 2-methylene-1,3-cyclopentanedione (1) that is compatible with acid-sensitive species. We have found that 1 is extremely reactive toward electron-rich alkenes, with the mode of reaction dependent on the alkene activation. For enamines and trimethylsilyl enol ethers, Michael addition leads to 2-substituted-1,3-cyclopentanediones. Alkyl enol ethers, on the other hand, form fused pyrans via concerted cycloaddition across the *s*-cis enone system of 1.

Experimental Section

Melting points were determined on a Fisher-Johns hot stage and are uncorrected. ^1H NMR spectra of solutions in $CDCl_3$ (with added pyridine-d_5 as noted) were obtained on a JEOL FX90Q (90 MHz) or a Nicolet NT-300WB (300 MHz) spectrometer. Chemical shifts are recorded in ppm downfield of internal TMS. ^{13}C NMR spectra were recorded on the JEOL FX90Q, operating at 22.5 MHz. Chemical shifts are referenced to the center line of the $CDCl_3$ multiplet (77.0 ppm). IR spectra (neat liquid films or KBr pellets, as noted) were recorded on a Nicolet 20 DXB FTIR; selected bands of interest are reported. Exact mass spectra were determined on a Kratos MS 25 spectrometer.

Ethoxyacetylene[16] and 1-methoxy-3[(trimethylsilyl)oxy]-1,3-butadiene[8] were prepared according to the published procedures. The stereolabeled ethyl vinyl ethers **16b,c** were synthesized by analogy to the method of Dombroski[15b] starting with ethoxyacetylene and D_2O, 99.8 atom % D (Aldrich).

Flash chromatography[17] was performed with Merck Kieselgel 60 (230–400 mesh), eluting with 65:35 (v/v) hexanes–acetone. Chloroform and pyridine were reagent grade, and ethyl ether was distilled from Na/benzophenone.

2-[(Phenylsulfinyl)methyl]-1,3-cyclopentanedione (2). A solution of 2-methyl-2-(phenylthio)-1,3-cyclopentanedione[2] (361 mg, 1.64 mmol) in dry ether (25 mL) was treated with *m*-chloroperoxybenzoic acid (360 mg, 79% titre, 1.0 equiv). The resulting solution was allowed to stand at room temperature for 3 h. After cooling to 0 °C to complete crystallization, the product was isolated by filtration (357 mg, 92%) and shown to be identical

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with material prepared by a slightly different procedure (ref 2b).

Additions to 2-Methylene-1,3-cyclopentanedione (1): General Procedure. The sulfoxide (2, 1 mmol) was suspended in chloroform (10 mL). Pyridine (1 mL) was added, and the mixture was stirred at room temperature until all solids were dissolved (3 min). The alkene (1.2 mmol) was added to this bright yellow solution, and stirring was continued for the required time interval (see Table I). The chloroform and most of the pyridine was removed in vacuo. The residue was partitioned between CH_2Cl_2 (20 mL) and 5% H_2SO_4, and the organic phase was dried over $MgSO_4$. After concentration, the crude product was purified as noted below.

2-(5-Methoxy-3-oxo-4-pentenyl)-1,3-cyclopentanedione (5) was crystallized from ethyl acetate (73% yield): mp >230 °C dec, IR (KBr) ν 3400–2600, 1647, 1615, 1580, 1373 cm^{-1}; ^1H NMR ($CDCl_3$, pyr-d_5) δ 7.64 (1 H, d, J = 13 Hz), 5.61 (1 H, d, J = 13 Hz), 3.65 (3 H, s), 2.70 (2 H, m), 2.50 (2 H, m), 2.46 (4 H, s); ^{13}C NMR 199.8, 194.8, 162.4, 115.8, 104.6, 56.8, 38.4, 29.8, 15.2 ppm; MS, m/e 210.0880, $C_{11}H_{14}O_4$ requires 210.0892.

3-Acetoxy-2-(3-oxobutyl)cyclopent-2-en-1-one (8). The crude product from reaction of 1 with 2-[(trimethylsilyl)oxy]-propene was stirred with acetic anhydride (0.5 mL) and triethylamine (0.5 mL) for 2 h. After concentration in vacuo, the residue was taken up in dichloromethane (10 mL), washed successively with 5% H_2SO_4 (5 mL) and saturated $NaHCO_3$ (5 mL), dried over $MgSO_4$, filtered, and concentrated. The product was purified by flash chromatography (49% yield, pale yellow oil): IR (neat) ν 1770, 1706, 1662 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.77 (2 H, m), 2.6–2.1 (8 H, m), 2.30 (3 H, s), 2.10 (3 H, s); ^{13}C NMR 206.5, 204.8, 175.7, 165.9, 127.5, 39.5, 33.6, 28.7, 26.2, 20.1, 15.4 ppm; MS, m/e 210.0874, $C_{11}H_{14}O_4$ requires 210.0892.

3-Acetoxy-2-[(2-oxocyclopentyl)methyl]cyclopent-2-en-1-one (9). The crude product from 1 and 2-[(trimethylsilyl)oxy]-cyclopentene was converted to the enol acetate as for 8 and isolated by flash chromatography (pale oil, 55%): IR (neat) ν 1773, 1735, 1704, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.85 (2 H, m), 2.50 (3 H, m), 2.30 (3 H, s), 2.3–1.7 (8 H, m); ^{13}C NMR 218.9, 205.0, 176.6, 166.2, 127.2, 46.6, 37.0, 33.9, 28.9, 26.5, 20.9, 20.5, 19.9 ppm; MS, m/e 236.1057, $C_{13}H_{16}O_4$ requires 236.1048.

2-[(2-Oxocyclopentyl)methyl]-1,3-cyclopentanedione (7). The crude product from reaction of *N*-cyclopentenylmorpholine and 1 was crystallized from ethyl acetate (yield, 68%): mp 131–134 °C; IR (KBr) ν 3400–2600, 1735, 1566, 1373 cm^{-1}; ^1H NMR ($CDCl_3$, py-d_5) δ 2.50 (4 H, s), 2.7–1.5 (9 H, m); ^{13}C NMR 222.9, 207.5, 115.3, 48.2, 37.6, 30.3, 29.5, 20.6, 20.1 ppm; MS, m/e 194.0920, $C_{11}H_{14}O_3$ requires 194.0943.

2,3,4,5,6,7-Hexahydro-3,3-dimethyl-5-oxocyclopenta[*b*]-pyran-2-ol (11): white crystals from hexanes–methyl *tert*-butyl ether; yield 60%; mp 122–123 °C; IR (KBr) ν 3200, 1679, 1607 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.4 (1 H, br s), 5.1 (1 H, br s), 2.51 (4 H, s), 2.06 (2 H, s), 1.00 (6 H, s); MS, m/e 182.0953, $C_{10}H_{14}O_3$ requires 182.0943.

3,4,4a,5,6,7,8,9a-Octahydrocyclopenta[*b*]pyrano[*e*]-2*H*-pyran-6-one (15): pale oil, purified by flash chromatography (60% yield): IR (neat) ν 1696, 1630, 1147, 1080, 1026 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.43 (1 H, d, J = 2.6 Hz), 3.80 (2 H, m), 2.7–1.9 (7 H, m), 1.62 (4 H, m); ^{13}C NMR 203.7, 182.2, 112.6, 99.8, 62.0, 33.1, 30.5, 25.7, 23.6, 23.3, 21.0 ppm; MS, m/e 194.0955, $C_{11}H_{14}O_3$ requires 194.0928.

2-Ethoxy-2,3,4,5,6,7-hexahydrocyclopenta[*b*]pyran-5-one (14): viscous oil, purified by flash chromatography (70% yield): IR (neat) ν 1695, 1635, 1107, 1042 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.33 (1 H, dd, J = 3.7, 2.6 Hz), 3.91 (1 H, dq, J = 9.7, 7.1 Hz), 3.69 (1 H, dq, J = 9.7, 7.1 Hz), 2.54, (2 H, m), 2.42 (2 H, m), 2.23 (2 H, m), 1.96 (1 H, m), 1.75 (1 H, m), 1.24 (3 H, t, J = 7.1 Hz); ^{13}C NMR 203.4, 181.6, 115.0, 100.5, 64.7, 32.9, 26.1, 25.5, 14.8, 12.6 ppm; MS, m/e 182.0952, $C_{10}H_{14}O_3$ requires 182.0943.

4a-Ethoxy-2,3,6,7,8,9,9a,10-octahydro-1*H*,4a*H*-cyclopenta[*b*]cyclopenta[5,6]pyrano[3,2-*e*]pyran-1,8-dione (18): isolated by flash chromatography; white solid (71%); mp 156–157 °C; IR (KBr) ν 1706, 1647 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.01 (2 H, q, J = 7 Hz), 2.7–1.9 (13 H, m), 1.24 (3 H, t, J = 7 Hz); ^{13}C NMR 202.9, 179.1, 115.8, 115.0, 58.8, 33.5, 30.5, 25.5, 20.3, 15.0 ppm; MS, m/e 290.1138, $C_{16}H_{18}O_5$ requires 290.1154.

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Synthesis of Oligosaccharides Corresponding to the Common Polysaccharide Antigen of Group B Streptococci†,[1]

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To facilitate mapping of the immunodominant region of the common polysaccharide antigen of group B streptococci, tetrasaccharide 1-*O*-{2-*O*-[2-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranosyl}-D-glucitol (**2**) was synthesized in a stepwise fashion, which was shown to be superior to the blockwise approach. The key glycosyl donor was methyl 2-*O*-acetyl-3,4-di-*O*-benzyl-1-thio-α-L-rhamnopyranoside (**22**), which was coupled to glycosyl acceptors via the agency of nitrosyl tetrafluoroborate. Other L-rhamnosyl donors developed were methyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (**13**), 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide (**28**), 2-*O*-acetyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl bromide (**30**), and 2-*O*-benzoyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl bromide (**33**). Also synthesized were 1-*O*-(α-L-rhamnopyranosyl)-D-glucitol (**3**), methyl 2-*O*-(α-L-mannopyranosyl)-α-L-rhamnopyranoside (**4**), 1-*O*-[2-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl]-D-glucitol (**5**), and methyl 2-*O*-[2-*O*-(α-L-mannopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranoside (**6**). The effect of the anomeric sulfur atom on the ^{13}C NMR parameters is discussed.

In spite of spectacular results in the development of antibiotics and other antimicrobial agents, morbidity and mortality rates of neonatal bacterial sepsis and meningitis are significantly high.[2] Major causative organisms of these diseases are encapsulated group B streptococci, which are classified into five serotypes based on their type-specific,

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